

I CLAIM:

Sub A

1. A tablet, comprising:
a core having (a) at least one active ingredient, and (b) a mixture of expandable materials, or greater than 25% of an expandable material, the expandable material or materials expanding upon exposure to an aqueous environment; and

an outer rupturable coating surrounding the core comprising a rate release modifying membrane and a water-soluble modifier.

Sub C1

2. The tablet according to claim 1 where the core comprises at least one hydrophilic gum material.

3. The tablet according to claim 1 further comprising an over coating of an active ingredient.

4. The tablet according to claim 1 where the tablet includes a belly band, at least a portion of the coating rupturing adjacent to or in the belly band upon exposure to an aqueous fluid.

5. The tablet according to claim 4 which produces a support platform for drug delivery.

6. The tablet according to claim 1 where the rate release modifying membrane contains one or more active ingredients.

7. The tablet according to claim 1 comprising pectin.

8. The tablet according to claim 7 where the pectin is low methoxy pectin.

9. The tablet according to claim 1 where the expandable material is an expanding

hydrophilic gum or mixture of hydrophilic gums.

10. The tablet according to claim 1 where the rate release modifying membrane is ethyl cellulose or a methacrylate polymer containing modifiers which influence active 5 ingredient release.

11. The tablet according to claim 4 where the belly band is the primary area exposed directly to hydrating fluids by rupture of the rate release modifying membrane.

10 12. The tablet according to claim 4 where the belly band area is from 0.1 to 1.0 of the tablet height measured at the tallest point.

15 13. The tablet according to claim 1 where the rate release modifying membrane is over coated or undercoated with an enteric coating material.

14. The tablet according to claim 1 where sustained release of an active ingredient following a lag time is sufficient to provide therapeutically effective active ingredient concentrations when administered in a once- or twice-daily dosing regimen.

20 15. The tablet according to claim 1 where dissolution of an active ingredient measured *in vitro* in a USP paddle stirring apparatus in appropriate aqueous media at 37°C, substantially corresponds to the following:

from 0 to 5% of the total active ingredient is released after one hour;

from 0 to 40% of the total active ingredient is released after four hours;

25 from 5 to 80% of the total active ingredient is released after eight hours; and not less than 70% of the total active ingredient is released in 24 hours.

16. The tablet according to claim 15 where the n value is 0.7 or more from time of

10% active ingredient released until time of 75% active ingredient released.

Sub A2

SUB A2
com

17. The tablet according to claim 15 where the n value is 0.85 or more from time of 10% active ingredient released until time of 85% active ingredient released.

5
SUB C1
18. The tablet according to claim 1 comprising a mixture of hydrophilic gum polymers, at least one of which is modified by enzymes in the intestinal tract.

10
19. The tablet according to claim 1 having a drug-delivery lag time of from about 0.5 hours or more and less than or equal to about 6 hours.

15
20. The tablet according to claim 1 having a drug delivery lag time of from about 1 to about 3 hours.

21. The tablet according to claim 18 where the hydrophilic gum polymer modified by enzymes in the intestinal tract is pectin.

22. The tablet according to claim 1 where the rate release modifying membrane is ethyl cellulose or a methacrylate polymer.

23. The tablet according to claim 4 where the belly band is between 1 and 8 mm thick and the length of the tablet is at least 8 mm.

24. The table according to claim 1 where the belly band is equal to or larger than a vertical height of the tablet as measured at a center portion of the tablet.

25. The tablet according to claim 4 where the rate release modifying membrane has been over coated with one or more active ingredients which may or may not exhibit a lag time for active ingredient dissolution.

30
SUB C1
26. The tablet according to claim 1 where calculated n value for average

dissolution results after a lag time is greater than at least 0.70 from time of 10% active ingredient released until time of 75% active ingredient released.

27. The tablet according to claim 1 where calculated n value for average dissolution results after a lag time is greater than at least 0.85 from time of 5% active ingredient released until time of 85% ingredient released.
28. The tablet according to claim 1 where the active ingredient is glipizide.
- 10 29. A spray-coated tablet according to claim 1.
- 15 30. The tablet according to claim 3 where dissolution of active ingredient from the overcoat and dissolution of active ingredient from the coated hydrophilic gum matrix core tablet is approximately zero order in that the calculated n value for average dissolution is greater than at least 0.70 from time of 10% drug released until time of 75% drug released.
- 20 31. The tablet according to claim 3 where dissolution of active ingredient from the coated hydrophilic gum matrix core tablet is approximately zero order, independent of drug release from the overcoat, in that the calculated n value for average dissolution is greater than 0.70 from time of 10% drug released until time of 75% drug released.
- 25 32. The tablet according to claim 3 where dissolution of the active ingredient from the overcoat plus dissolution of active ingredient from the coated hydrophilic gum matrix core tablet is approximately zero order in that the calculated n value for average dissolution result is greater than 0.85 from time of 5% drug released until time of 85% drug released.
- 30 33. The tablet according to claim 3 where dissolution of the active ingredient from the coated core tablet is approximately zero order, independent of drug release from the overcoat, in that the calculated n value for average dissolution result is greater than 0.85 from time of 5% drug released until time of 85% drug released.

Sue A. Cerny 5

34. The tablet according to claim 3 wherein there is a burst dissolution of active ingredient(s) from the over-coated materials, and then the calculated n value for average dissolution results for at least one active ingredient released from the coated core tablet after the lag time is greater than at least 0.70 from time of 10% release of the active ingredient in the core tablet is released until time of 75% of the active ingredient in the core tablet is released

10 35. A tablet, comprising:
one or more active ingredients;
a mixture of hydrophilic gum polymers where the mixture comprises between about 40% and 95% by dry weight of the tablet ingredients, the mixture comprising at least one hydrophilic gum polymer which is modified by enzymes in the intestinal tract;
at least one excipient which promotes powder mixture flow; and
a spray coating over the external surface of the tablet, the coating comprising a rupturable rate release controlling membrane.

15 36. The tablet according to claim 35 wherein the hydrophilic gum polymer which is modified by enzymes in the intestinal tract is pectin.

20 37. A spray-coated tablet which exhibits a lag time for active ingredient dissolution, comprising:
glipizide;
a mixture of hydrophilic gum polymers comprising at least one hydrophilic gum polymer which is modified by enzymes in the intestinal tract; and
25 a rate release controlling membrane overcoating the mixture.

30 38. The tablet according to claim 37 wherein the hydrophilic gum polymer which is modified by enzymes in the intestinal tract is pectin.

39. The tablet according to claim 37 where the rate controlling membrane is ethyl

T017200 "34522/8860

cellulose or a methacrylate polymer.

40. The tablet according to claim 37 where at least one hydrophilic gum is hydroxypropyl methyl cellulose, the hydrophilic gum polymer which is modified by enzymes in the intestinal tract is pectin, and the rate controlling membrane comprises ethyl cellulose or a methacrylate.

41. The tablet of claim 37 where, during hydration with aqueous fluids, the hydrophilic polymer gum core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the hydrophilic gum polymer core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film occurs.

42. The tablet according to claim 37 having a belly band between about 1 and about 8 mm thick and the length of the tablet is at least 8 mm.

43. The tablet according to claim 37 where the belly band of the tablet is equal to or larger than vertical height of the tablet as measured at the center of the tablet.

44. The tablet according to claim 37 having a first rate controlling membrane, and wherein the first rate controlling membrane has been over coated with a second rate release controlling membrane, at least one of the rate release controlling membranes being an enteric coating membrane.

45. The tablet according to claim 37 where the rate controlling membrane has been over coated with one or more active ingredients which may be the same or different from the active ingredients in the core tablet, and wherein the release of the active ingredient may or may not exhibit a lag time for active ingredient dissolution.

46. The tablet according to claim 37 where dissolution of the active ingredient is

NOV 20 2001 FEB 2 2002 FEB 24 2002

approximately zero order in that the calculated n value for average dissolution results after the lag time is greater than 0.70 from time of 10% drug released until time of 75% drug released.

47. The tablet according to claim 37 where dissolution of the active ingredient is approximately zero order in that the calculated n value for average dissolution results after the lag time is greater than 0.85 from time of 5% drug released until time of 85% drug released.

48. The tablet according to claim 37 wherein dissolution of the active ingredient is approximately zero order in that the calculated n value for average dissolution results after the lag time is greater than 0.70 from time of 10% drug released until time of 75% drug released.

49. The dosage form of claim 37 wherein dissolution of the active ingredient is approximately zero order in that the calculated n value for average dissolution results after the lag time is greater than 0.85 from time of 5% drug released until time of 85% drug released.

50. A tablet which exhibits a lag time for active ingredient dissolution, comprising:
one or more active ingredients;
a mixture of hydrophilic gum polymers comprising between about 40% and about 95%
by dry weight of all tablet ingredients, the mixture comprising at least one hydrophilic gum
polymer which is modified by enzymes in the intestinal tract and at least one excipient which
promotes powder mixture flow and attracts water; and
an outer rupturable coating comprising a rate release controlling membrane.

51. The tablet of claim 50 wherein the hydrophilic gum polymer which is modified
by enzymes in the intestinal tract is pectin.

52. A barrier coated tablet which generates a support platform *in situ*, the barrier
coated tablet having a drug dissolution versus time curve with a lag time of between 0.5 and 3
hours, an n value of 0.85 or greater, and where a k value is between 0.04 and 0.25.

53. A barrier coated tablet which generates a support platform *in situ*, the barrier coated tablet having a drug dissolution versus time curve with a lag time of between 0.5 and 3 hours, an n value of 0.85 or greater, and the k value is between 0.05 and 0.1.

5 54. A tablet, comprising:
a core comprising an active ingredient, and an enzymatically modifiable, expandable material which expands upon exposure to an aqueous environment; and
an outer rupturable rate release modifying membrane, the tablet providing active ingredient release over at least a 16-hour period.

10 55. A tablet having a drug-delivery lag time, comprising:
a core comprising an active ingredient, a water-soluble modifier gum and at least one second expandable gum which expands upon exposure to an aqueous environment; and
an outer rupturable rate release modifying membrane over coating the core.

15 56. The tablet according to claim 55 where the active ingredient is glipizide.

57. A spray coated tablet according to claim 55.

20 58. The tablet of claim 1 where, during hydration with aqueous fluids, the expandable material core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film.

25 59. The tablet of claim 33 where, during hydration with aqueous fluids, the hydrophilic polymer gum core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the hydrophilic gum polymer core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film occurs.

30

PCT/US2000/0160

Sub
A

60. The tablet of claim 50 where, during hydration with aqueous fluids, the core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film.

61. The tablet of claim 52 where, during hydration with aqueous fluids, the core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film.

62. The tablet of claim 53 where, during hydration with aqueous fluids, the core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film occurs.

63. The tablet of claim 54 where, during hydration with aqueous fluids, the core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film occurs.

64. The tablet of claim 55 where, during hydration with aqueous fluids, the core tablet swells and ruptures the rate controlling membrane which breaks away from part of the tablet and exposes portions of the core tablet, and remains attached to portions of the tablet providing a support platform for at least two hours after initial breaking of the polymer release rate controlling film occurs.

100-200-300-400-500-600-700-800-900

65. The tablet according to 52 where dissolution of active ingredient from the overcoat and dissolution of active ingredient from the coated core tablet is approximately zero order in that the calculated n value for average dissolution is greater than 0.70 from time of 5 10% drug released until time of 75% drug released.

66. The tablet according to claim 52 where dissolution of active ingredient from the coated core tablet is approximately zero order, independent of drug release from the overcoat, in that the calculated n value for average dissolution is greater than 0.70 from time of 10% drug 10 released until time of 75% drug released.

67. The tablet according to claim 52 where dissolution of the active ingredient from the overcoat plus dissolution of active ingredient from the coated core tablet is approximately zero order in that the calculated n value for average dissolution result is greater than 0.85 from 15 time of 5% drug released until time of 85% drug released.

68. The tablet according to claim 52 where dissolution of the active ingredient from the coated core tablet is approximately zero order, independent of drug release from the overcoat, in that the calculated n value for average dissolution result is greater than 0.85 from 20 time of 5% drug released until time of 85% drug released.

69. The tablet according to 53 where dissolution of active ingredient from the overcoat and dissolution of active ingredient from the coated core tablet is approximately zero order in that the calculated n value for average dissolution is greater than 0.70 from time of 25 10% drug released until time of 75% drug released.

70. The tablet according to claim 53 where dissolution of active ingredient from the coated core tablet is approximately zero order, independent of drug release from the overcoat, in that the calculated n value for average dissolution is greater than 0.70 from time of 10% drug 30 released until time of 75% drug released.

TOTDOD-062101-00002860

71. The tablet according to claim 53 where dissolution of the active ingredient from the overcoat plus dissolution of active ingredient from the coated core tablet is approximately zero order in that the calculated n value for average dissolution result is greater than 0.85 from time of 5% drug released until time of 85% drug released.

72. The tablet according to claim 53 where dissolution of the active ingredient from the coated core tablet is approximately zero order, independent of drug release from the overcoat, in that the calculated n value for average dissolution result is greater than 0.85 from time of 5% drug released until time of 85% drug released.

73. A method for administering an active ingredient, comprising:
providing a tablet comprising a core having an active ingredient and an expandable material which expands upon exposure to aqueous environment, the core surrounded by an outer rate release modifying membrane which ruptures upon exposure to aqueous environment;
and
administering the tablet to a patient.

74. A method for administering an active ingredient, comprising:
providing a tablet comprising one or more active ingredients, a mixture of hydrophilic gum polymers where the mixture comprises between about 40% and 95% by dry weight of the tablet ingredients, the mixture comprising at least one hydrophilic gum polymer which is modified by enzymes in the intestinal tract, at least one excipient which promotes powder mixture flow, and a spray coating over the external surface of the tablet, the coating comprising a rupturable rate release controlling membrane; and
administering the tablet to a patient.

75. A method for administering an active ingredient, comprising:
providing a tablet comprising glipizide, a mixture of hydrophilic gum polymers comprising at least one hydrophilic gum polymer which is modified by enzymes in the

TOP SECRET//DEFENSE

SUB
C1

intestinal tract, and a rate release controlling membrane overcoating the mixture; and administering the tablet to a patient.

76. A method for administering an active ingredient, comprising:
5 providing a tablet comprising one or more active ingredients, a mixture of hydrophilic gum polymers comprising between about 40% and about 95% by dry weight of all tablet ingredients, the mixture comprising at least one hydrophilic gum polymer which is modified by enzymes in the intestinal tract and at least one excipient which promotes powder mixture flow and attracts water, and an outer rupturable coating comprising a rate release controlling 10 membrane; and

administering the tablet to a patient.

77. A method for administering an active ingredient, comprising:
15 providing a barrier coated tablet which generates a support platform *in situ*, and a drug dissolution versus time curve with a lag time of between 0.5 and 3 hours, an n value of 0.85 or greater, and where a k value is between 0.04 and 0.25; and
administering the tablet to a patient.

78. A method for administering an active ingredient, comprising:
20 providing a barrier coated tablet which generates a support platform *in situ*, the barrier coated tablet having a drug dissolution versus time curve with a lag time of between 0.5 and 3 hours, an n value of 0.85 or greater, and the k value is between 0.05 and 0.1; and
administering the tablet to a patient.

25 79. A method for administering an active ingredient, comprising:
providing a tablet, the tablet comprising (a) a core comprising an active ingredient and an expandable material which expands upon exposure to an aqueous environment, and (b) an outer rupturable rate release modifying membrane, the tablet providing active ingredient release over at least a 16-hour period; and
30 administering the tablet to a patient.

*Sub
C1*

80. The method according to claim 79 where the expandable material is enzymatically modifiable.
81. A method for administering an active ingredient, comprising: providing a tablet having a core comprising an active ingredient, a water-soluble modifier gum and at least one second expandable gum which expands upon exposure to an aqueous environment, and an outer rupturable rate release modifying membrane over coating the core; and
- 10 administering the tablet to a patient.
82. The tablet according to claim 1 where the outer rupturable coating includes a water-insoluble modifier.
- 15 83. A tablet, comprising:
a core having (a) at least one active ingredient, and (b) a mixture of expandable materials, or greater than 25% of an expandable material, the expandable material or materials expanding upon exposure to an aqueous environment; and
an outer rupturable coating surrounding the core comprising a rate release modifying membrane and a film modifier.
- 20
84. The tablet according to claim 83 where the rate release modifying membrane is ethyl cellulose or a methacrylate polymer containing modifiers which influence active ingredient release.
- 25 85. A method for administering an active ingredient, comprising:
providing a tablet which exhibits a lag time for active ingredient dissolution from a core, the tablet comprising a core having an expandable material which expands upon exposure to an aqueous environment, at least one active ingredient, and an outer rupturable coating surrounding the core comprising a rate release modifying membrane and a film modifier; and

administering the tablet to a patient, the tablet thereafter undergoing hydration so that, during hydration of the tablet, the core swells and ruptures the rate release modifying membrane which breaks away from part of the tablet and exposed portions of the core, and remains attached to portions of the tablet providing a support platform for at least two hours when tested 5 *in vitro* after initial rupture of the rate release modifying polymer occurs.

86. The tablet according to claim 15 where from 20 to 80% of the total active ingredient is released after eight hours.

10 87. The tablet according to claim 15 where not less than 80% of the total active ingredient is released in 24 hours.

Cela
A6